Registratie en kwantitatieve interpretatie van kleurstofverdunningscurves, verkregen door reflectiemeting in rood of infrarood licht.

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SUMMARY

Chapter I

Some historical aspects of the injection method for the investigation of the circulation of the blood are reviewed. Major events have been the development of Stewart's procedures I and II for measuring the cardiac output by continuous respectively instantaneous injection of an indicator [97] (equations 1 and 2) and the introduction of a method to differentiate once-circulated from twice-circulated dye by semilogarithmic extrapolation of the descending limb of the primary curve by Hamilton[48] (fig. 17).

Several investigators pioneered with the injection method and improved it. Henriquez [40] discovered the effects of recirculation. Bock and Buchholtz[3] stressed the importance of injection at a constant rate when applying Stewart's procedure I and of collection at a constant rate when applying procedure II. Romm[87] published the first continuously recorded NaCl dilution curve, made by means of a capillary electrometer. With the introduction of ear and cuvette oximeters for use as continuous dye densitometers a great impetus was received. The direct motive for this thesis has been the introduction of reflection oximetry by Brinkman et al.[4, 5, 6] and the possibility of using this method in dye dilution techniques.

Chapter II

The apparatus, by which light reflecting from a layer of blood, either in the skin or in a cuvette, is measured, consists of a measuring eye, a galvanometer and switch-box, all pertaining to the CC oximeter and a cuvette, a sampling device for rapid and constant withdrawal of blood from an artery, and a recorder.

The measuring eye of the CC oximeter is sensitive to light of $\lambda =$ 600-700 $m\mu$ and in this range most blue dyes can easily be detected.

Another measuring eye, sensitive to a wave band around $\lambda = 800\ m\mu$ has been specially developed for measuring infrared absorbing dyes.

The CC oximeter cuvette proved to be unsuitable for recording dye dilution curves. A satisfactory change was the development of a cuvette consisting of polyvinylchloride tubing with a constant inner diameter (fig. 27).

A suction device serves for withdrawal of blood at a constant rate of 0.76 ml/sec. Blood is prevented from entering the Luer-Lok syringe by a slack rubber membrane which is introduced into a vessel between cuvette and syringe (figs. 4 and 6). This system is perfused with heparinized 5% glucose solution, when no blood is being withdrawn.

The curves can be recorded adequately with suitable galvanometers and a photokymographion or with direct writing apparatus like the Kipp Micrograph BD 3 or the Sanborn Polyviso 150 M with chopper preamplifier 150-1500 and adaptorbox 461-142.

Directions for use are given at length.

Chapter III

To fulfill the requirements of the injection method a dye must be: *a.* strongly absorbing the light to which the measuring apparatus is sensitive; *b.* unchanged while in the blood; *c.* eliminated from the circulation within a few hours, although the dye should not disappear from the blood in any significant amount in the short period, necessary to accomplish one full circulation; *d.* non toxic.

On account of the light absorption spectra of different dyes, methylene blue and patent blue V proved to be the most suitable (requirement *a.* fig. 8). Methylene blue is a rapidly diffusing dye. Patent blue V is being eliminated from the blood within a few hours (fig. 14). The properties of the two dyes are discussed. Fox' green is the only commercially available infrared absorbing dye suitable for studies of the circulation. Its instability in aqueous solutions is a minor drawback (fig. 15).

Chapter IV

The dye particles injected into the bloodstream will behave as if they were natural constituents of the blood. As the particles injected within one second will take several seconds to pass the measuring site downstream, they do not travel all at the same rate. The mean transit time $\bar{t}$ can be computed, which is the x-coördinate of the centre of gravity of

the area under the dilution curve. The central bloodvolume can be found by multiplying the cardiac output by $\bar{t}$ (equation 8).

The nomenclature proposed by Wood and Swan [113] is adopted (fig. 16), but not the symbols suggested by these authors, because some are confusing. We introduced an extrapolated zero concentration time which is the time from the moment of injection to T_d. T_d is found by semilogarithmic extrapolation of the descending limb of the primary curve to the level of one percent of the peak concentration. The moment of injection is in the origin of the coördinate system.

If the curve is to be confidently interpreted quantitatively, stress must be laid on the passage of all injected dye past the ostium aortae. Stagnation of the injected dye can occur in several ways, e.g. by stasis in a vein just after injection, by stasis near the vessel wall when laminary flow prevails, by circus movement through a *left→right* shunt or by flow up and down an insufficiently closed ostium.

Chapter V

The factors that determine the shape of and the area under the curve are discussed.

The relationship of the dye concentration in the blood to the amount of light reflected (galvanometer deflection) is rendered graphically by fig. 20. Although the relationship is not strictly linear, up to a concentration of 10 mg dye per liter of blood it may be approximated by a straight line. This holds true for all the dyes we tested. Variations in hemoglobin concentration will have no influence on the area of the curve, since the light reflection is virtually independent of the total hemoglobin concentration above 8 g%.

As a matter of fact the oximeter measuring eye is very sensitive to variations in the oxygen saturation of the blood. As a rule the oxygen saturation of arterial blood will not fluctuate, but in some cases it varies with respiration. If measurements are performed in a spectral band around the isobestic point of hemoglobin and oxyhemoglobin ($\lambda = 805\ m\mu$), variations in the oxygen saturation will not be visible in the curve. With this in view our infrared measuring eye has been developed.

Tabel I shows that after the injection of a small amount of patent blue V there is an apparent decrease in the oxygen saturation of the blood. This disturbs oximetry. The apparent decrease in the oxygen saturation of the blood after the injection of small amounts of Fox' green is far less, as can be seen in tabel II. Oximetric data are still

reliable after Fox' green dilution curves have been made, provided that small amounts of dye have been used.

Chapter VI

The calibration of the dilution curves done after Nicholson and Wood[78], McNeely and Gravallese[67] and Emanuel et al[17], i.e. the calibration of the y-axis for mg of dye/l blood, is an essentially static method.

In contrast, we introduced a dynamic calibration procedure in which a dilution curve obtained in a circulation model filled with the patient's blood is compared with the curve of the patient. Both curves are made under exactly the same conditions with the same apparatus. The sampling device, described in chapter II serves as a model. The flow in the model (Q_c) is known. When I_c mg of dye is injected into the model just beyond the arterial needle a dye dilution curve can be recorded in the cuvette. The area (A_c) under this calibration curve in mm² can be related to Q_c and I_c by the Stewart Hamilton formula, thus

$$Q_c = \frac{I_c}{A_c}$$

The area under the calibration curve in mm² has now been calibrated in mg.min/l The area under the patient's curve (A) is related to the amount of dye injected into the patient (I) and the cardiac output (Q) by the equation:

$$Q = \frac{I}{A}$$

Dividing Q by Q_c gives:

$$Q = \frac{I.A_c.Q_c}{A.I_c} \tag{7}$$

where Q is the cardiac output in l/min.,

A and A_c are the areas under the patient's curve respectively calibration curve in mm²,

I and I_c are the amounts of dye injected into the patient respectively into the model in mg or, more conveniently, in ml of the same dye solution.

To obtain a properly measurable area under the calibration curve the fluid volume between the arterial needle and the cuvette has to be increased by a sort of capillary bed. For this purpose a piece of polyethelene tubing, filled with polyethylene beads is used. The area under the curve does not change by this addition, although the curve becomes lower and wider. How cardiac output and central bloodvolume are calculated from the patient's curve and calibration curve is shown in fig. 38 and 39.

A modification of the forward-triangle procedure admits a rapid but approximative calculation of the cardiac output immediately after the curves have been recorded (equation 10).

Chapter VII

Data on the comparison of cardiac output values, obtained by the Fick and Stewart Hamilton methods are reviewed[15,27,39,84,85,90,109]. All authors agree that in the majority of cases the differences do not exceed 25%.

Richardson et al.[84] found a standard deviation of 12.5% between the two methods. In no case the difference was greater than 25%. The reproducibility of the Fick method was not better than that of the Stewart Hamilton procedure. The authors also found that curves obtained by injection into the vena mediana cubiti and into the pulmonary artery are equally reliable, provided the dye is immediately flushed into the central circulation by a following glucose injection.

The determination of the cardiac output by the Fick procedure requires right heart catheterisation. In this way the average output over a period of five or six minutes is measured. The Stewart Hamilton procedure requires only puncture of a vein and artery and the average output over a few heart beats is determined. The procedure can be repeated quickly. When the dynamic calibration procedure, described in chapter VI, is employed no laboratory work is involved as distinct from the Fick procedure.

Chapter VIII

It is once more stressed that for the diagnosis of abnormal flow patterns in the central circulation by a series of dye dilution curves a sufficiently rapid response of the apparatus is of paramount importance. The apparatus described in chapter II has been developed with the purpose to meet this requirement. The curves obtained with the aid of it show

a good resolving power, i.e. abnormal peaks may be clearly distinguished from normal ones.

The case histories, catheterisation data and dye dilution curves of 6 patients are discussed. When an abnormal pathway in the central circulation preferentially drains the blood from a certain vessel, that vessel should be selected for the injection of dye in order to obtain a maximum effect on the dilution curve and thus most reliable diagnostic information.

For example the blood from the vena cava inferior will be shunted preferably to the left atrium by a secundum type of atrial septal defect. The sinus venosus type of atrial septal defect, however, will preferably shunt the blood from the vena cava superior. Preferential shunting of blood from the right lung in contrast to that from the left lung takes place when an atrial septal defect with a left to right shunt exists, at least in the majority of cases (case 2). Abnormally draining lung veins often can be easily detected by a series of dye dilution curves (cases 5 and 6).